REMARKS

I. Preliminary Remarks Regarding Amendments

The Applicants do not intend by any amendments to abandon the subject matter of any claim previously presented. The Applicants reserve the right to pursue the subject matter of such claims during prosecution of this or subsequent applications. Claims 1, 3-24, and 31-33 stand rejected and are currently being examined. Claims 1 and 3-6 are canceled herein, and claims 7-12, 14-24, and 31 are amended herein. Thus, claims 7-24 and 31-33 are currently pending.

II. Amendments

The Applicants have inserted a claim to priority of two U.S. provisional patent applications that were co-pending at the time the present application was filed.

Support for the amendment to claims 7-12, 14-18, and 20-24 can be found at least at page 37, Table 1, and at page 5, lines 7-15. Claim 31 is amended to appropriately reflect pending claims.

Pursuant to 37 C.F.R. §1.121, a marked-up version of the amendment to the specification and claims made herein is attached hereto as Appendix A. For the convenience of the Examiner, also attached, as Appendix B, is a copy of claims 7-24 and 31-33 as they read upon entry of the present amendment.

The amendment includes no new matter.

III. Patentability Arguments

A. The Scope of Enablement Rejection of Claims 1, 3-6, and 31-33 under 35 U.S.C. § 112, First Paragraph, May Properly Be Withdrawn.

Claims 1, 3-6, and 31-33 stand rejected for reciting subject matter assertedly not described in the specification in a manner sufficient to enable any person skilled in the art to make and use the invention commensurate in scope with the claims. The Examiner holds that the specification does not reasonably disclose formulation of vaccines for "any" gram-negative bacteria that comprises "any" mutation in SEQ ID NO: 3 or a species homolog

thereof for the induction of a protective response and asserts that Applicants do not fully enable the genus of vaccine compositions. While Applicants respectfully disagree, Applicants concede claims 1 and 3-6 herein rendering the rejection moot. As indicated in paragraph 4 of the Office Action, claims 7-24 and 31-33 are enabled by the specification. Applicants respectfully request withdrawal of the rejection.

B. The Written Description Rejection of Claims 1 and 3-33 under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn.

The rejection of claims 1 and 3-33 under 35 U.S.C. §112, first paragraph, is maintained for assertedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the invention. The Office Action asserts that no specific genes that encode species homologues of the identified nucleic acid sequences meet the written description requirement by providing an adequate number of species of the claimed genus of mutations in species homologues of SEQ ID NO: 3. The Applicants respectfully disagree.

The first paragraph of 35 U.S.C. §112 requires that the specification set forth a written description of the invention. The purpose of the "written description" requirement is to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991); *see also Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568, 43 U.S.P.Q.2d 1398, 1405 (Fed. Cir. 1997). The invention is, for purposes of the "written description" inquiry, whatever is claimed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991).

The Applicants contend that the Examiner has applied the written description analysis that is specifically applicable for nucleic acids and that this analysis is not appropriate for all "genus" subject matter. The claimed invention relates to attenuated gram-negative bacteria and vaccine compositions comprising the bacteria and **not** to polynucleotides *per se*. The specification discloses that *Pasteurellaceae* bacteria comprising a mutation that decreases atpG activity are attenuated and useful in vaccines. The specification discloses that such a mutation may take many forms, e.g., *see* specification at p. 5, line 7 to p.

6, line 10. In light of the present disclosure, one of skill in the art would recognize that the inventors were in possession of the claimed invention at the time of filing.

For example, the specification provides exemplary embodiments with two species of gram-negative attenuated *Pasteurellaceae* bacterial atpG genes, the *P. multocida* atpG gene in SEQ ID NO: 3 and the *A. pleuripneumonia* atpG gene in SEQ ID NO: 132. The Applicants are not claiming specific mutations to the polynucleotide sequence of atpG, but rather are claiming attenuated *Pasteurellaceae* bacterial strains resulting from a mutation in the atpG gene. The specification clearly shows that mutations in atpG genes result in attenuation of the bacteria which is an effective vaccine in both mice and pigs (see specification at pp. 31-53, Examples 1-11). Furthermore, the Applicants have described the identification of atpG genes in other gram-negative bacterial species (*see* specification at pp. 39-41, Example 5).

With this disclosure, the Applicants have fully described every common feature that every species in the claimed genus must possess. The claimed bacteria share the common features of being of the family *Pasteurellaceae* bacteria, comprise a mutated atpG gene, and have reduced atpG product activity. There is no need to precisely define the chemical structure of every atpG gene in every bacteria or vaccine. Indeed, there is **no** need for such a description as evidenced by the fact that only attenuation of a strain by mutation (i.e. the end result) is important. The precise chemical change to the atpG coding region is irrelevant.

In view of the above considerations and the amendments to the claims, one would recognize that the Applicants were in possession of the necessary common features or attributes possessed by members of the genus. Thus, Applicants submit that the rejection should properly be withdrawn.

C. The Indefiniteness Rejections of Claims 1, 3-24 and 31-33 under 35 U.S.C. §112, Second Paragraph, May Properly Be Withdrawn.

The Examiner maintains the rejection of claims 1, 3-24 and 31-33 under 35 U.S.C. §112, second paragraph, as assertedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner rejects claims 1, 3-24 and 31-33 and asserts that the amendment to the claims to recite a mutation in the atpG protein coding region partially obviates the

rejection, but does not fully clarify what gene product must evidence decreased activity or decreased expression. Applicants submit that the amendment to claim 7 to recite "resulting in decreased atpG biological activity" clarifies that the claims encompass attenuated *Pasteurellaceae* bacteria wherein both decreased biological activity and decreased expression are covered. Thus, the rejection of claims 7-24, and 31-33 under 35 U.S.C. §112, second paragraph, should properly be withdrawn. Applicants concede claims 1 and 3-6 herein rendering the rejection moot as it relates to those claims.

The rejection of claims 8, 14 and 20 under 35 U.S.C. §112, second paragraph, was maintained for the reason of record in paper 15, for assertedly including two mutations in the gene product. The Applicants submit that the present amendment to claims 8, 14 and 20 to recite a "bacteria of claim 7 wherein the activity is decreased due to decreased gene expression of an atpG gene product encoded by the mutated atpG protein coding region" obviates the Examiner's rejection, and as such the rejection of claims 8, 14 and 20 under 35 U.S.C. §112, second paragraph should properly be withdrawn.

The Examiner also rejected claims 31-33 for depending from non-elected claims. The Applicants submit that the amendment to claim 31 to depend from "any one of claims 7-24" obviates the Examiner's objection to the recitation of non-elected inventions in the claims.

The Applicants submit that the claims set forth the subject matter and particularly point out and distinctly define the metes and bounds of the subject matter which Applicants regard as the invention. Therefore, the Applicants submit that the various rejections under 35 U.S.C. § 112, second paragraph, for asserted indefiniteness, should properly be withdrawn.

D. The Anticipation Rejection of Claims 1, 3-5 and 31-32 under 35 U.S.C. §102(b), May Properly Be Withdrawn.

Claims 1, 3-5, and 31-32 under 35 U.S.C. § 102(b), stand rejected as allegedly being anticipated by the disclosure of Nakamoto. Cancellation of claims 1 and 3-5 and the amendment of claim 31 to depend from claims 7-24 render the rejection moot. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102(b).

IV. CONCLUSION

In view of the amendments and remarks made herein, Applicants respectfully submit that claims 7-24 and 31-33 are in condition for allowance and respectfully request expedited notification of same. Should the Examiner have any questions of form or substance, she is welcomed to contact the undersigned at the telephone number below.

Respectfully submitted,

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APPENDIX A

Version Marked to Show Changes

In the Specification

At page 1, line 4:

This application claims benefit of U.S. Provisional Patent Application Serial Nos.: 60/128,689, filed April 9, 1999, and 60/153,453, filed September 10, 1999.

In the Claims

1. [CANCELED]

3. [CANCELED]

4. [CANCELED]

5. [CANCELED]

6. [CANCELED]

7. (Twice Amended) An attenuated *Pasteurellaceae* bacteria comprising a mutation in the atpG protein coding region set forth in SEQ ID NO: 3 or a species homolog thereof, said mutation resulting in decreased atpG biological activity ~~of a gene product encoded by the mutated gene~~, wherein the decreased atpG biological activity attenuates the *Pasteurellaceae* bacteria.

8. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein the decreased atpG biological activity is decreased due to decreased gene expression ~~said mutation results in decreased expression of a~~ of an atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

9. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in expression of an inactive atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

10. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in deletion of all or part of said atpG gene.

11. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in deletion of at least about 10%, at least about 20%, at least about 30%, at least about 40% at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, or at least about 99% of said atpG gene.

12. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in an insertion in the atpG gene, said insertion causing decreased expression of a an

atpG gene product encoded by the mutated atpG protein coding region ~~gene~~ and/or expression of an inactive atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

14. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein the decreased atpG biological activity is due to decreased gene expression ~~said mutation results in decreased expression of a~~ of an atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

15. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in expression of an inactive atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

16. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in deletion of all or part of said atpG gene.

17. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in deletion of at least about 10%, at least about 20%, at least about 30%, at least about 40% at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, or at least about 99% of said atpG gene.

18. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in an insertion in the atpG gene, said insertion causing decreased expression of ~~a~~ an atpG gene product encoded by the mutated atpG protein coding region ~~gene~~ and/or expression of an inactive atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

20. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein the decreased atpG biological activity is decreased due to decreased gene expression ~~said mutation results in decreased expression of a~~ of an atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

21. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in expression of an inactive atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

22. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in deletion of all or part of said atpG gene.

23. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in deletion of at least about 10%, at least about 20%, at least about 30%, at least about 40% at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, or at least about 99% of said atpG gene.

24. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in an insertion in the gene, said insertion causing decreased expression of ~~a~~ an atpG gene product encoded by the mutated atpG protein coding region gene and/or expression of an inactive atpG gene product encoded by the mutated atpG protein coding region ~~gene~~.

31. (Twice Amended) An immunogenic composition comprising the bacteria according to any one of claims ~~1 through~~ 7-24.

APPENDIX B

Pending Version of Claims after Amendment

7. (Twice Amended) An attenuated *Pasteurellaceae* bacteria comprising a mutation in the atpG protein coding region set forth in SEQ ID NO: 3 or a species homolog thereof, said mutation resulting in decreased atpG biological activity, wherein the decreased atpG biological activity attenuates the *Pasteurellaceae* bacteria.

8. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein the decreased atpG biological activity is decreased due to decreased gene expression of an atpG gene product encoded by the mutated atpG protein coding region.

9. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in expression of an inactive atpG gene product encoded by the mutated atpG protein coding region.

10. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in deletion of all or part of said atpG gene.

11. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in deletion of at least about 10%, at least about 20%, at least about 30%, at least about 40% at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, or at least about 99% of said atpG gene.

12. (Amended) The *Pasteurellaceae* bacteria of claim 7 wherein said mutation results in an insertion in the atpG gene, said insertion causing decreased expression of a an atpG gene product encoded by the mutated atpG protein coding region and/or expression of an inactive atpG gene product encoded by the mutated atpG protein coding region.

13. The *Pasteurellaceae* bacteria of claim 7 selected from the group consisting of *Pasteurella haemolytica*, *Pasteurella multocida*, *Actinobacillus pleuropneumoniae* and *Haemophilus somnus*.

14. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein the decreased atpG biological activity is due to decreased gene expression of an atpG gene product encoded by the mutated atpG protein coding region.

15. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in expression of an inactive atpG gene product encoded by the mutated atpG protein coding region.

16. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in deletion of all or part of said atpG gene.

17. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in deletion of at least about 10%, at least about 20%, at least about 30%, at least about 40% at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, or at least about 99% of said atpG gene.

18. (Amended) The *Pasteurellaceae* bacteria of claim 13 wherein said mutation results in an insertion in the atpG gene, said insertion causing decreased expression of ~~a~~ an atpG gene product encoded by the mutated atpG protein coding region and/or expression of an inactive atpG gene product encoded by the mutated atpG protein coding region.

19. The attenuated *Pasteurellaceae* bacteria of claim 13 that is a *P. multocida* bacteria.

20. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein the decreased atpG biological activity is decreased due to decreased gene expression of an atpG gene product encoded by the mutated atpG protein coding region.

21. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in expression of an inactive atpG gene product encoded by the mutated atpG protein coding region.

22. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in deletion of all or part of said atpG gene.

23. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in deletion of at least about 10%, at least about 20%, at least about 30%, at least about 40% at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 98%, or at least about 99% of said atpG gene.

24. (Amended) The *Pasteurellaceae* bacteria of claim 19 wherein said mutation results in an insertion in the gene, said insertion causing decreased expression of ~~a~~ an atpG gene product encoded by the mutated atpG protein coding region gene and/or expression of an inactive atpG gene product encoded by the mutated atpG protein coding region.

31. (Twice Amended) An immunogenic composition comprising the bacteria according to any one of claims 7-24.

32. A vaccine composition comprising the immunogenic composition according to claim 31 and a pharmaceutically acceptable carrier.

33. The vaccine composition according to claim 32 further comprising an adjuvant.